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10/551,203	06/29/2006	Simon Michael West	024944-9015-00	4056

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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,203	WEST ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-18 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9-18 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/24/09, 06/19/09, 12/15/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Receipt of Applicants Arguments/Remarks and **RCE** all filed on 06/19/09 is acknowledged.

Claims **8 and 19-20** remain cancelled.

Claims 1-7, 9-18 and 21-25 are pending in this application and **claims 1-7, 9-18 and 21-25** will be prosecuted on the merits.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-4, 6-7, 9-18 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kirby et al. U.S.Patent No. 6,444,234 B1 (herein after '234) in view of WO 02/40033 A1 (herein after '033) and further in view of Vaghefi et al.(US PG pub 2003/0157326).

Kirby et al. discloses pharmaceutical compositions for the transdermal administration of a medicament or active agent by topical application of the composition to the skin of humans or animals (abstract).

'(234) teaches a method for formulating safe and effective compositions for topical transdermal applications of an active agent such as morphine (column 5 lines 3-5 and col. 42 example 14). (It should be noted that Morphine has tertiary amine as claimed in claim 1)The composition as set forth by ('234) comprises an active agent in a "carrier". Said "carrier" comprises solvent and modifying agents. The solvent modifiers facilitate the dissolution of the active agent and formation of the weak association which enable the complex of active agent-modifier to pass the defensive of the skin with minimal irritation without modification of the chemical structure or stereoscopic configuration of the active agent (column 11, lines 5-10). The solvent modifiers selected do not form permanent or strong covalent bonds with the medicament or active agents; instead they form complexes that facilitate the movement of the complex past the viable skin to its targeted site (column 5 lines 53-

56).

Although (‘234) discloses the use of solvent modifiers in formulating pharmaceutical compositions for the transdermal administration of a medicament or active agent, (‘234) does not explicitly teach using phosphate derivatives of tocopherol or other tocols as claimed in the instant application as solvent modifiers for the same purpose.

WO 02/40033 A1 ('033) teaches an efficacious therapeutic emulsion formulation for therapeutic administration comprising phosphate derivatives of “electron transfer agents” and an “acceptable carrier” (abstract).

According to ('033), the use of a phosphorylated electron transfer agent plays therapeutic and efficacious role in dermal penetration (page 3, lines 3-8).The “electron transfer agents” as indicated by ('033), refer to the class of chemicals, which may be phosphorylated.

Examples of classes of “electron transfer agents” that may be phosphorylated include hydroxyl chromans including alpha, beta and gamma tocopherol, tocols and tocotrienols in enantiomeric and racemic forms; quinols being the reduced form of vitamin K1 and ubiquinone; hydroxyl carotenoids including retinol and ascorbic acid (page 3, lines 26-28 and page 4, lines 1-2). The phosphate derivatives may exist in the form of a free phosphate acid, a salt thereof, a di-phosphate ester thereby including two molecules of electron transfer agents, a mixed ester including two different compounds selected from electron transfer agents, or a phosphatidyl compound (page 4, lines 5-9).

('033) further teaches that the phosphate derivatives of “electron transfer agents” can be combined with ‘acceptable carrier”.

As defined in (‘033), the “acceptable carrier” could be referred to a “carrier” considered by those skilled in the drug, food or cosmetic arts to be non-toxic when used to treat humans, animals or plants in parenteral or enteral formulations. The “carrier” will depend on the route of administration and the ingestible formulations, which include tablets, capsules, powders etc. (see page 4, lines 30-33 and page 5, lines 1-6). (‘033) further teaches that phosphate derivative may exist in the form of a phosphatidyl compound wherein the free phosphate oxygen forms a bond with an alkyl group or a complex with a complexing agent selected from amphoteric surfactant, cationic surfactant or aminoacids having nitrogen functional groups or proteins rich in these amino acids (see page 4, lines 8-11 and claim 4).

‘033 teaches electron transfer agents comprising phosphate complexes of tocopherol, the usefulness of these compounds in therapeutic formulations due to their enhanced absorption properties (see full document, specifically Page 3, line 22-Page 4, line 2, Page 5, paragraph 3-Page 6, paragraph 5, Pages 7-9, Example 2, Table 1).

Vaghefi et al. while disclosing absorption enhancing pharmaceutical compositions and methods, teach tocopherol phosphate as bio enhancer (see page 5 paragraph {0045]). Vaghefi et al. further disclose that small molecule drugs that exhibit limited bioavailability in humans and that are capable of being formulated into a higher bioavailable composition and used to provide better bioavailability are administration

include alkaloids such as codeine, fentanyl and quinine etc. (see page 9, paragraph [0094]).

(Instant specification teaches that most alkaloids are not water soluble. Typically alkaloids are a class of drugs that are not commonly administered transdermally because the hydrophilic nature of alakaloid salts usually limits transdermal transport. (See page 2, lines 10-15).

Based on the foregoing, it would have been obvious to one of ordinary skilled in the art at the time of the invention to use the phosphate derivatives of tocopherol ('033) in the compositions of ('234) comprising an alkaloid such as morphine or any other alkaloid such as codeine, fentanyl and quinine. One skilled in the art would have been motivated to utilize tocopherol phosphate with alkaloid because '033 teaches electron transfer agents comprising phosphate complexes of tocopherol, the usefulness of these compounds in therapeutic formulations due to their enhanced absorption properties (see full document, specifically Page 3, line 22-Page 4, line 2, Page 5, paragraph 3-Page 6, paragraph 5, Pages 7-9, Example 2, Table 1) and Vaghefi et al. teaches compositions of drugs with limited bioavailability (for instance codeine, fentanyl etc. which are known alkaloids) comprising bioenhancers such as tocopherol phosphate. Formulation of reaction product complex of morphine (or any other alkaloid) and tocopherol phosphate (electron transfer agent) would have been obvious to one of ordinary skilled in the at the time of instant invention based on the teachings of '033 which teaches unexpected absorption properties of the drug and Vaghefi et al. which teaches absorption enhancing composition of drugs with limited bioavailability

comprising bioenhancers such as tocopherol phosphate with a reasonable expectation of success.

Response to Arguments

4. Applicant's arguments filed 06/19/09 have been fully considered but they are not persuasive.

Applicant argues that prima facie case of obviousness has not been made. Applicants have submitted declaration and quote that Applicants submit herewith the West Declaration, and note that the declarant, Dr. Simon Michael West, is also the sole inventor of Tocovite and, therefore, is uniquely situated to attest to what one of skill in the art would or would not have been motivated to do, particularly, in light of his Tocovite patent. Dr. West's comments on the development surrounding Tocovite, as well his opinion regarding the motivation Tocovite might or might not provide are found in paragraphs 6-8 of the West Declaration, and have not been recited herein for the sake of brevity. These portions of the West Declaration, however, are very useful in understanding the context of Tocovite and how it relates with the other cited references.

Applicants further argue that opinion of Dr. West as provided in the declaration clearly shows that one of ordinary skill in the art would and have been motivated to combine the references. First applicants arguments and opinions in the declaration are not persuasive because the declaration does not provide any experimental evidence to substantiate the opinion. The declaration only provides opinion why one of ordinary would not combine the prior art. It is to be noted that Applicants motivation to combine the references do not have to be similar to Examiner's motivation to combine the references.

Applicants have provided individual merits of the prior art, however, the Examiner recognizes that it must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references, which make up the state of the art with regard to the claimed invention. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). The examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references In re Nomiya, 184 USPQ 607 (CPA 1975). However, there is no requirement that an "express, written motivation to combine must appear in prior art references before a finding of obviousness." See Ruiz v. A.B. Chance Co., 357 F.3d 1270, 1276, 69 USPQ2d 1686, 1690 (Fed. Cir. 2004). For example, motivation to combine prior art references may exist in the nature of the problem to be solved (Ruiz at 1276, 69 USPQ2d at 1690) or the knowledge of one of ordinary skill in the art (National Steel Car v. Canadian Pacific Railway Ltd., 357 F.3d 1319, 1338, 69 USPQ2d 1641, 1656 (Fed. Cir. 2004)). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969).

In the instant case, Kirby has been cited for complex formation of alkaloid with solvent modifiers and utilization in transdermal administration of morphine. '033 teaches electron transfer agents comprising phosphate complexes of tocopherol, the usefulness of these compounds in therapeutic formulations due to their enhanced absorption properties (see full document, specifically Page 3, line 22-Page 4, line 2, Page 5, paragraph 3-Page 6, paragraph 5, Pages 7-9, Example 2, Table 1). The reference also teaches complexation of phosphate derivative of tocopherol with amino acids having nitrogen functional groups and proteins rich in amino acids. As such the reference teaches complexing phosphate derivative of tocopherol with active ingredients including amines.

Vaghefi has been combined for the teachings of phosphorylated electron transfer agents in increasing bioavailability and as supported by instant specification (Instant specification teaches that most alkaloids are not water soluble. Typically alkaloids are a class of drugs that are not commonly administered transdermally because the hydrophilic nature of alkaloids salts usually limits transdermal transport. (See page 2, lines 10-15). As such based on the teachings of prior art, one would have been motivated to combine the teachings of the prior art and come to the claimed invention with a reasonable expectation of success absent evidence to the contrary and unexpected results.

Given the teachings of the prior arts it would have been obvious to try and make complex of phosphate derivative of electron transfer agent with any therapeutic drug of

choice, particularly drugs having tertiary amine groups, at the time the invention was made.

When there is motivation

> to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under [35 USC] 103.

KSR Int'l Co. v. Teleflex Inc., 127 S.Ct 1727,-----, 82 USPQ2d 1385, 1397 (2007).

Alternatively, the therapeutic compounds and phosphate derivatives of tocopherol are not applicant's invention. They are in the public domain prior to the time the instant invention was made. Applicant has done no more than combine separate but well-known inventions. While the combination may perform a useful function it did no more than what they would have done separately. *In re Anderson,* 396 U.S. 57, 163 USPQ 673 (1969) cited in *KSR Int. Co. v. Teleflex Inc*, 550 U.S. ----, 82 USPQ2d 1385 (2007). When a patent simply arranges old elements with each performing the same function it had been known to perform and yields predictable result, the combination is obvious. *In re Sakraida,* 425 US 273, 189 USPQ 449 (1976) cited in *KSR, supra.* A patent for such combination "obviously withdraws what is already known into the field of

its monopoly." *Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp.,* 340 U.S. 147, 187 USPQ 303 (1950), cited in *KSR, supra.*

"When a work is available in one field of endeavour, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technology is obvious unless its actual application is beyond his or her skill." "One of the ways in which a patent's subject matter can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims." *KSR Int. Co. v. Teleflex Inc*, 550 U.S. ----, 82 USPQ2d 1385 (2007).

Response to Declaration

5. The declaration under 37 CFR 1.132 filed 06/19/09 is insufficient to overcome the rejection of claims **1-7, 9-18 and 21-25** based upon 35 USC 103 as set forth in the last Office action because: The declaration only states the opinion of Dr. West regarding the merits of individual reference and Dr. west only provides his expert opinion about how one of ordinary would not consider combining phosphate derivative of tocopherol with active ingredient comprising tertiary amine. There are no experimental evidence provided to substantiate the same. Arguments of counsel cannot take the place of

factually supported objective evidence. See, e.g., In re Huang, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 168 (Fed. Cir. 1996); In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed.Cir. 1984).

The declaration on page 2, paragraph 8 states that: In my opinion, the disclosure in Tocovite would not motivate one of skill in the art to include alkaloids in those formulations, although the **use of alkaloids would not be precluded**. Again, my focus in developing Tocovite was on enhancing the dermal penetration and/or efficacy of mono-electron transfer agent phosphate derivatives.

Applicant's arguments are not persuasive because applicant himself admits that use of alkaloids would not have been precluded based on the teachings of Tocovite reference.

The declaration further asserts that Kirby's theory excludes sulfate and phosphate derivatives because they were not considered to efficiently transfer through the skin and thus would not have been considered appropriate or suitable for such formulations.

This argument is not substantiated by evidence, as such is not persuasive.

The declaration further provides opinion that Tocovite would not have suggested modifying the formulations of Kirby to arrive at the claimed invention. In particular, one of skill in the art would not have been motivated by Tocovite to 1) phosphorylate the solvent modifiers of Kirby, 2) use water as a solvent, rather than the ethanol/propylene glycol solvent of Kirby, or 3) remove the forskolin of Kirby. Furthermore, in my opinion, phosphorylating Kirby's solvent modifiers, e.g., lemon oil (or/and d-limonene), Vitamin E, Pro-Vitamin B, D-panthenol and methylsulfonylmethane (MSM), (Kirby col. 11, Ins. 11-14) would not achieve the efficacy of the claimed alkaloid formulations. This is because the Stock Delivery System of Kirby is highly unsuitable for use with sulfate or phosphate derivatives of hydrophobic substrates.

Applicants arguments are not persuasive because Kirby has been cited only to combine with morphine which is an alkaloid and Kirby discloses topical and transdermal application of morphine. Tocovite has been cited for adding tocopherol phosphate to morphine because of its enhanced solubility properties disclosed by Tocovite.

The declaration further assets that Vaghefi's process is different from the claimed invention and thus would not have motivated to combine the teachings with Kirby and Tocovite reference.

Applicant's arguments are not persuasive because the motivation for combining tocopherol phosphate is for its property of being bioenhancer as stated in Vaghefi, Vaghefi is not cited for process cited in the reference. It is respectfully pointed out that the declaration only provides opinion which is not substantiated by experimental evidence to prove the same.

6. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Kirby et al. U.S.Patent No. 6,444,234 B1 (herein after '234) in view of WO 02/40033 A1 ("033), Vaghefi et al..(US PG pub 2003/0157326) and further in view of Fisher et al. (US 2004/0234602 A1).

The references discussed above do not teach using enteric coatings in the oral formulations.

However, Fischer et al. in US publication (U.S. 2004/0234602 A1) discloses a composition with enteric coating and a method for controlling the release of a therapeutically active substance from a pharmaceutical composition into an aqueous medium, wherein the pharmaceutical composition is a coated matrix composition in which the matrix comprises:

Polymer or mixture of polymers,
An active substance and optionally,
One or more excipients
(Page 1, paragraph 1)

The polymers such as polyethylene oxide or eudragit L methyl ester as disclosed by Fischer et al. (on page 3, paragraph 41 and 43) are an example of enteric coatings. The active substance such as morphine, codeine and atropin can be used in the above composition (page 4, paragraph 51) in an oral formulation (page 3, paragraph 48). ('172) further teaches that in order to soften the "carrier system", a plasticizer can be selected from group of phosphate esters for e.g. a-tocopherylphosphate esters (page 8 paragraph 100).

Because Fischer et al. teaches that enteral coatings can be used to control release of drug and since it is well known in the art that enteral coatings are used to promote absorption of drugs in the intestine, it would have been obvious to one of ordinary skilled in the art at the time the invention was made to use enteric coatings as taught by Fischer et al. in the teachings advanced by Kirby et al. as modified by ('033) and Vaghefi et al.. A skilled artisan would be motivated to prepare enteric-coated oral formulations of alkaloids such as morphine or atropine complexed with phosphate derivatives of "electron transfer agents" or in other words phosphate derivatives of tocopherol with reasonable expectations of success because enteric coatings help in the absorption of the active substance in the intestine.

Response to Arguments

7. Applicant's arguments filed 10/14/08 have been fully considered but they are not persuasive.

Applicant has not argues this reference specifically, the rationale for combining the prior art has been discussed above which renders the claimed invention obvious to one of ordinary skill in the art at the time of the instant invention.

New Rejections

8. Claims 1-7, 9-18 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over West et al. (WO 02/40034 A1 (herein after '034), presented in IDS.

West '034 teaches composition comprising phosphate derivatives of hydroxylated compounds and complexing agents. West discloses phosphate derivative of tocopherol improves tissue penetration, see page 4, lines 23-24. West discloses electron transfer agents such as tocopherol phosphate complexed with active ingredients such as one containing nitrogen as functional group and others are more soluble, see page 9, lines 3-5. West discloses forming complex with tocopherol phosphate and tertiary amine achieve more bioavailability in oral or injectable formulation, see page 9, lines 5-10. codeine is discloses on page 9, lines 18. Electron transfer agents are vitamin K1, retinol, calciferol etc. on page 10, lines 15-17. Examples of complexing agents are disclosed on page 11, lines 25-30. The formulation can be in the form of lotion and creams, see page 13, lines 19-20.

The difference between the instant invention and that of the prior art is that applicant compositions comprise specific therapeutic agents.

However, the generic compounds of West '034 embrace the specific therapeutic compounds by applicant. Making phosphate derivative of any therapeutic drug is an obvious modification available to the preference of an artisan. Therefore, the instant invention is prima facie obvious from the teachings of the prior arts. One of ordinary skill in the art would have known to make phosphate derivative of any therapeutic drug of choice at the time the invention was made. The motivation is from the teachings of the prior art.

Alternatively, given the teachings of the prior art it would have been obvious to try and make phosphate derivative of any therapeutic drug of choice, particularly drugs having tertiary amino group or alkaloids at the time the invention was made.

When there is motivation

> to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under [35 USC] 103.

KSR Int'l Co. v. Teleflex Inc., 127 S.Ct 1727,-----, 82 USPQ2d 1385, 1397 (2007).

Alternatively, the therapeutic compounds, phosphate and complexing agents are not applicant's invention. They are in the public domain prior to the time the instant invention was made. Applicant has done no more than combine separate but well-

known inventions. While the combination may perform a useful function it did no more than what they would have done separately. *In re Anderson,* 396 U.S. 57, 163 USPQ 673 (1969) cited in *KSR Int. Co. v. Teleflex Inc*, 550 U.S. ----, 82 USPQ2d 1385 (2007). When a patent simply arranges old elements with each performing the same function it had been known to perform and yields predictable result, the combination is obvious. *In re Sakraida,* 425 US 273, 189 USPQ 449 (1976) cited in *KSR, supra.* A patent for such combination "obviously withdraws what is already known into the field of its monopoly." *Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp.,* 340 U.S. 147, 187 USPQ 303 (1950), cited in *KSR, supra.*

Alternatively, given the teachings of the prior arts one would have known to make compositions comprising phosphate derivatives of any compounds having tertiary amine group at the time the invention was made. "When a work is available in one field of endeavour, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technology is obvious unless its actual application is beyond his or her skill." "One of the ways in which a patent's subject matter can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims." *KSR Int. Co. v. Teleflex Inc*, 550 U.S. ----, 82 USPQ2d 1385 (2007).

Alternatively, applicant has done nothing more than substitutes therapeutic drugs with tertiary amine group. However, such substitution is obvious from the prior arts. "When a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result." *United States v. Adams,* 383 U.S. 49, 50-51 (1966). Cited in *KSR Int. Co. v. Teleflex Inc*, 550 U.S. ----, 82 USPQ2d 1385 (2007). The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR, supra.*

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business

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/Snigdha Maewall/
Examiner, Art Unit 1612
/Gollamudi S Kishore/
Primary Examiner, Art Unit 1612